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Topical Review

Pulmonary calcifications: a review

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Pulmonary calcification is a common asymptomatic finding, usually discovered on routine chest X-ray or at autopsy.

Pulmonary calcifications are caused mainly by two mechanisms: the dystrophic form and the metastatic form (1). Despite the different aetiologies, the pulmonary function and clinical manifestations are quite similar in both forms. We present a review of the clinical and radiology findings of the different aspects of pulmonary calcifications according to its pathogenesis and its anatomic distribution: parenchymal, lymphe node and pleural.

Key words: pulmonary calcifications; tuberculosis; hyperparathyroidism; chronic renal failure; pulmonary nodules.

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Parenchymal pulmonary calcifications

DYSTROPHIC FORM (TYPE)

Dystrophic calcifications occur in a damaged lung following an inflammatory process such as infection (tuberculosis, histoplasmosis, *Pneumocystis carnii*), bleeding or pulmonary infarction (2,3). It is a local, organized process with local deposition of crystalline hydroxyapatite calcium salt. By definition, the serum level of calcium and phosphate is normal. The most frequent causes are healed primary granulomatous lesions (Ghon focus) which consist of a densely calcified focus situated anywhere in the lung, commonly in the upper lung fields and benign tumours like hamartoma (25–30%) (4). The Ghon focus, which is usually a part of the Ranke complex (calcified hilar or mediastinal lymph node) establishes the diagnosis of previous infection (tuberculosis, histoplasmosis in endemic areas, coccidioidomycosis or other fungal infections). Multiple punctate calcifications in the spleen may aid in the diagnosis of histoplasmosis.

Chest radiograph and computed tomography (CT) are usually specifics and permit identification of the character of the calcification which can be an important indicator of the aetiology. A central nidus is a sign of a granulomatous lesion (Fig. 1), lamination is pathognomonic of granuloma, popcorn-ball calcification is characteristic of hamartoma (Fig. 2) and multiple punctate lesions throughout a lesion may be seen in either granulomas or hamartoma. Usually, calcifications in a pulmonary nodule are indicative of a benign process, but there are some exceptions: carcinoma may grow from an old calcified granuloma (in this case, the calcification is eccentric), or it may be a natural process of metastatic osteogenic sarcoma and chondrosarcomas (5) (Fig. 3).

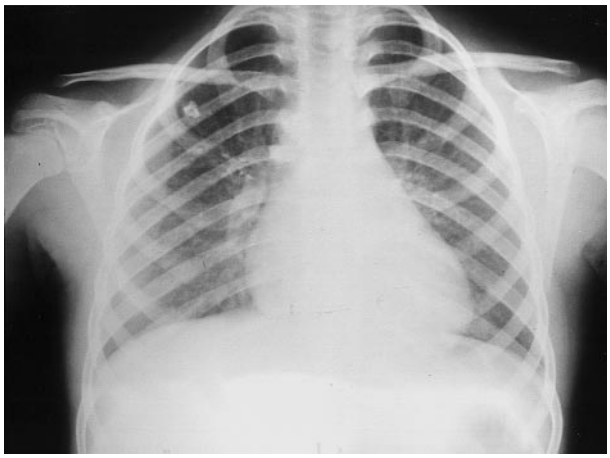

FIG. 1. Ghon focus; calcified granulomatous lesion in the right upper lobe.

METASTATIC CALCIFICATIONS

Metastatic calcifications are caused by high levels of serum calcium and phosphate which deposit in normal lung tissue. The common aetiologies are primary or secondary hyperparathyroidism, chronic renal failure and neoplastic destructive bony lesions like multiple myeloma (6–8).

In these settings, calcifications can occur in any tissue of the body but commonly deposit in the lungs, kidney and

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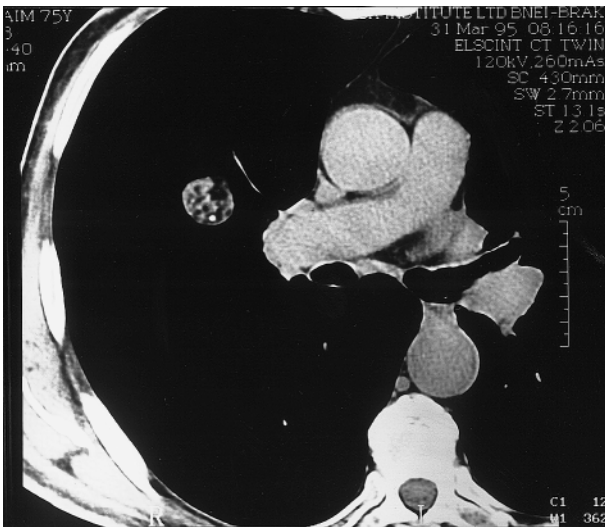

FIG. 2. Popcorn ball calcification in hamartoma.

FIG. 3. Adenocarcinoma with eccentric calcifications.

stomach (tissues with alkaline pH). In the lungs, calcifications usually deposit in the interstitium of the alveolar septum, the walls of the bronchioles and pulmonary vessels, or in the large airways (Fig. 4). The upper lobes are mainly involved because of the higher ventilation–perfusion ratio producing a lower end capillary PCO_2 and a higher pH, while the relatively bases lobes have a higher end-capillary PCO_2 and then a lower pH (9).

The clinical manifestations of pulmonary calcifications are usually minimal but occasionally may cause dyspnoea. Therefore, they are rarely diagnosed because of their benign clinical course. No correlation is found between the extent of macroscopic calcifications and the clinical symptomatology: massive calcifications can be completely asymptomatic.

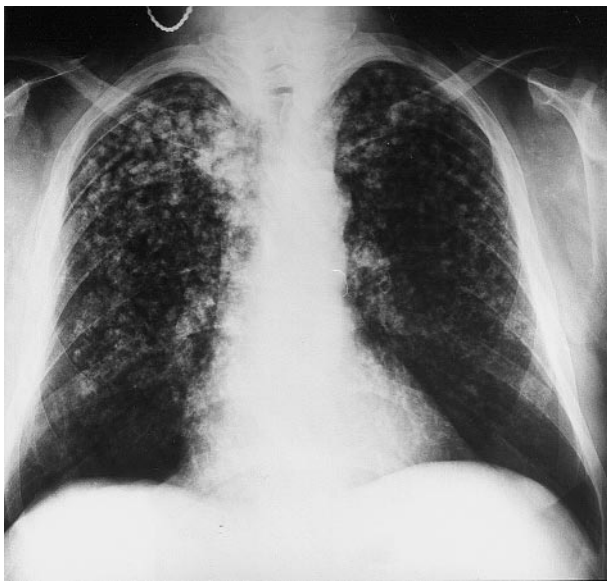

FIG. 4. Pulmonary metastatic calcifications in a haemodialysis patient.

When comparing between normal, chronic renal failure and parathyroidectomized dogs, the role of parathyroid hormone (PTH) and high calcium levels has been demonstrated in the genesis of pulmonary calcifications (10). Within the chronic renal failure group, the incidence of metastatic calcification is higher in the chronic haemodialysis group (60–75%) and the correction of hypercalcaemia or parathyroidectomy can reverse the calcification process (11).

Asymptomatic pulmonary calcification is a well known complication of patients following orthoptic liver transplantation. The cause is thought to be metabolic (12,13). Because of the associated coagulopathy, patients receive a large amount of fresh frozen plasma which contains sodium citrate: (1200 mg per unit in fresh frozen plasma and 100 mg sodium citrate per unit in packed red cells). This results in a high plasma citrate level which leads to metabolic alkalosis and hypocalcaemia by chelation of ionized calcium. The parathyroid hormone secretion is then triggered and, when a large amount of exogenous calcium is administered, subsequently calcium is deposited in soft tissues. Ectopic calcifications appear immediately or in the early months following the liver transplant. In a retrospective review of autopsies, Watchell *et al.* found ectopic calcifications in 84% of cases post liver transplantation, which was correlated with the amount of calcium and blood product administration during the transplant course. Others studies by Munoz and Jensen confirm these findings (14–16).

Chest radiographs and CT scan findings are not specific and may be misleading. The infiltrates can be diffuse or localized, usually composed of small nodules. However, patchy or confluent consolidation mimicking air space disease has been described (17–19). The relative stability of these pulmonary infiltrates, in contrast to infectious processes, is of diagnosis value. However, as these patients are highly immunosuppressed, infection should always be excluded.

In chronic renal failure patients, the extent of pulmonary calcification correlates poorly with the serum calcium and phosphorus levels, the aetiology of renal disease, the length of dialysis and the degree of parathyroid hyperplasia.

Some reports have demonstrated the ability of technetium 99m labelled bone scanning radionuclides to detect pulmonary calcification (20–22). The scan shows an increased uptake in the lungs, even in the absence of radiographical abnormalities.

This leads some authors to advise scintigraphy as part of the evaluation of dyspnoea in patients with chronic renal failure. Sullivan *et al.* reported lung uptake of TC-99m as well as of gallium–67 in a patient with lymphoma and hypercalcaemia (23). It has been suggested that calcium deposition in the interalveolar septa potentiates GA 67 uptake in the lungs. Abnormal uptake of TC-99m supports this suspicion and obviates the need for an invasive diagnostic procedure.

Regardless of the aetiology and the organ affected, calcifications are seen on haematoxylin and eosin slides as a granular, lamellar and plate-like basophilic materials that stains positively with Von Kassa and Alizarin red stains (24).

Pleural calcifications

Pleural calcifications occur most often as the result of long standing inflammatory diseases, like haemothorax, empyema or induced pneumothorax for tuberculosis (Fig. 5). The disease is usually unilateral, and is associated with thickening of the visceral pleura. The calcification occurs in the inner aspect of the pleural thickening, is extensive and sheet-like.

Pleural calcification is also a common manifestation of asbestos exposure. Forty years after exposure, over 50% of patients have radiologically visible pleural plaques which calcified within several years of becoming evident radiologically (Fig. 6). The calcification is seen as a dense, discontinuous white line paralleling the chest wall, the diaphragm or the cardiac border, and involves the parietal pleura (25–27). The roentgenological abnormalities could be easily distinguished between the two. The CT is highly sensitive in the demonstration of calcium in pleural plaques (28).

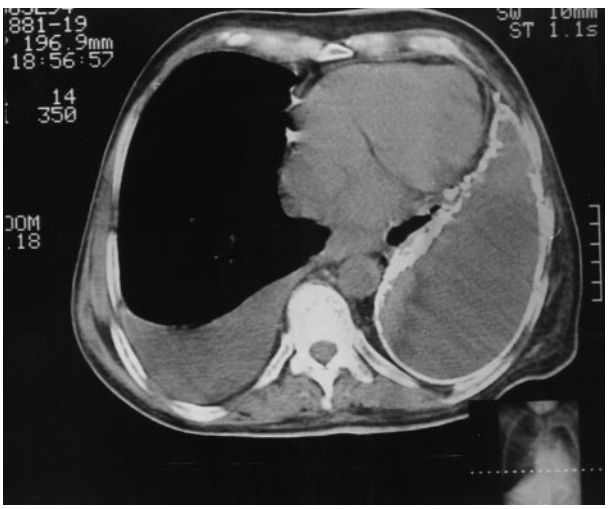

FIG. 5. Calcified pleura secondary to a long standing pleural effusion.

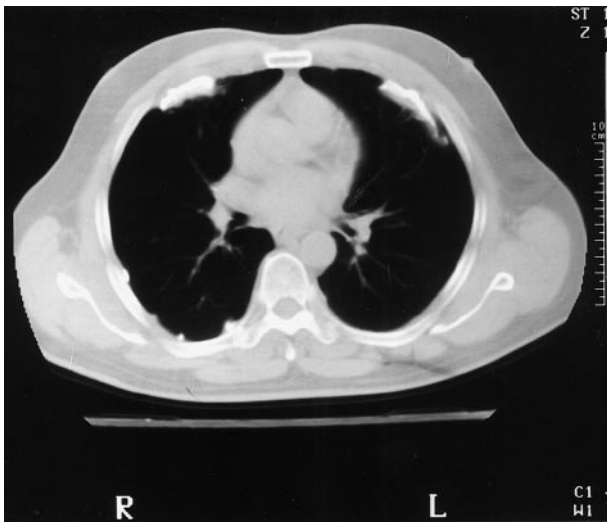

FIG. 6. Pleural plaques in asbesto.

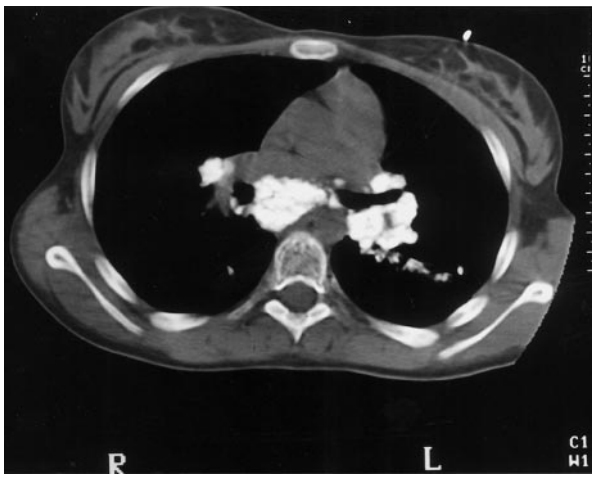

FIG. 7. Bilateral lymph node calcifications in sarcoidosis.

Lymph node calcification

Foci of calcification in lymph nodes are usually irregularly distributed throughout the node. They result from healed granulomatous infection, usually tuberculosis or histoplasmosis and constitute part of the Ranke complex. They have little clinical significance but they can erode a contiguous airway causing bronchiolithiasis with haemoptysis and chronic cough (Fig. 7).

Another variety of nodal calcification is the Eggshell calcification, which appears as a dense ring around the periphery of a lymph node. It is highly suggestive of silicosis or coal workers' pneumoconiosis, but it has been described also in sarcoidosis (Fig. 7), Hodgkin's disease or infections like histoplasmosis or blastomycosis (29).

Conclusion

Pulmonary calcification is a common finding on chest X-ray and chest CT. Knowing the various aetiologies and radiological differences may help in the differential diagnosis and may eliminate the need for unnecesary invasive procedures.

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